REMARKS

Claims

Claims 1–6, 9, 10, 13 and 14 are pending of which claims 10, 13 and 14 are withdrawn from consideration. Claims 7–8 and 11–12 were previously cancelled without prejudice or disclaimer. Claim 15 is added by this paper.

Amendments

Claim 1 has been amended. Support for the amendment can be found, for example, in Example 3 of the originally-filed application.

New claim 15 is supported, at least, by the disclosure contained in the Examples.

It is respectfully submitted that the amendments do not recite new matter. Entry thereof is respectfully requested.

Election of species

Applicants thank the Examiner for extending the election of species to include molecules that allow detection of the expression of cell-surface CD154. See, item 10 of the Office Action.

Formal objections

The objection of the specification for allegedly failing to provide a BRIEF DESCRIPTION OF THE DRAWINGS is respectfully traversed. Applicants submit that the present specification provides a detailed description of each of all the drawings. See, for example, the detailed description of each drawing in the Examples section of the specification. Moreover, as explicitly stated under §608.01(a), the outlining and/or arrangement of the specification into discrete sections is merely "preferred" and not mandatory as alleged in the Office Action. Withdrawal of the objection is respectfully requested.

The objection of the specification for allegedly reciting trademarks is moot in view of the amendments.

The specification has been amended to recite the relationship of the present application to the international application.

Withdrawal of the objection is respectfully requested.

Rejections under §112

The rejection of claim 1 under this section for allegedly failing to recite clear and definitive method steps for allegedly being incomplete is respectfully traversed. The Office Action at page 5

alleges that the claim term "detecting the expression of CD154" is indefinite. At page 6 of the Office Action, a similar argument is made with respect to the rejection of claims 1–6 and 9 under §112, ¶1 (enablement). Applicants respectfully disagree with these contentions.

The present specification provides explicit guidance on the nature of CD154 molecules, including techniques and reagents that may be employed in the detection of the expression thereof. To this end, the specification for example, in the paragraph bridging pages 7 and 8, discloses that CD154 is expressed on CD4+ T cells and detection thereof may be made without undue experimentation. The specification further teaches that the art is replete with information on methods and reagents for the detection of CD154 on cell surface, as evidenced by the referenced articles by Berner et al. (2000) and Schonbeck et al. (2000). Moreover, insofar as methods for detecting changes in gene expression (i.e., mRNA levels) and gene-product expression levels (i.e., protein levels) are known in the art, a skilled worker can employ any routine technique, for example nucleic acid hybridization assays and/or antibody-based detection assays for practicing the claimed invention in its broadest possible scope. To this end, the present specification provides a detailed description of at least two embodiments, which may be utilized in the detection step. For example, at page 13 of the specification, a direct methodology for detection of CD154 (e.g., FACS sorting or magnetic cell sorting) is described. See also, Example 3 of the specification wherein CD154-expressing T cells are detected and isolated using FACS. In page 14, ¶2, the specification provides an indirect method of detecting CD154 expression, wherein the *in vivo* effects of non-functional CD154 expression is described. As such, the PTO's contentions regarding indefiniteness are without merit.

Under items 6 and 8 of the Office Action, it is alleged that CD40 is <u>not</u> expressed extracellularly in vital T-cells, and as such, the claimed subject matter is indefinite and/or non-enabled. These contentions are respectfully traversed. Since the Office Action has not presented evidence to support the allegations, the rejections based thereon are legally misplaced. In any event, Applicants have amended the claim to recite method steps that allow a skilled worker to practice the claimed invention in its broadest possible scope. Applicants' amendment of the claims is not to be construed as acquiescence to this or any other ground of rejection. Withdrawal of the rejection is respectfully requested.

<u>Art rejections</u>

The rejection of claims 1–6 and 9 under §102(b) as being anticipated by Assenmacher et al. (WO 99/58977) is respectfully traversed. The rejection appears to be based on the Patent Office's contention that the cited reference teaches detection of antigen-specific T cells in patients suffering

from inflammatory conditions using CD154/CD40 specific antibodies. While Assenmacher may disclose a method for the detection of antigen-specific T cells comprising employing CD40-specific antibodies, the cited reference is absolutely silent with respect to the detection of CD154, as recited in the present claims. More specifically, the reference is silent regarding the use of a CD154-specific antibody for the detection of said CD154. See, new claim 15. As such Assenmacher cannot anticipate the claims of the present application. It is required that for anticipation, the reference publication teach, either explicitly or inherently, all the elements of Applicants' claims. Absent such, there can be no anticipation.

The rejection under of claims 1–6 and 9 under §102(b) as being anticipated by Berner (2000) and/or Batataglia (1999) is respectfully traversed. The Examiner contends that the references' disclosure of detection of antigen-specific T-cells from patients with rheumatoid arthritis and/or Crohn's disease meets all the elements of claims 1–6 and 9. See, page 8 of the Office Action. Applicants submit that the forgoing amendments render these rejections moot. More specifically, neither Berner nor Batataglia teach a method for isolating antigen-specific T cells comprising employing a CD40/CD154 system inhibitor which blocks or inhibits the interaction between CD40 and CD154 and detecting the expression of CD154. Additionally, the mere assertion that CD154 molecules are expressed in T-cells is insufficient for anticipation of the present claims. The Office Action has not established that CD154 molecules are in fact detected in these patients. As such these rejections are legally misplaced.

Withdrawal of the rejection is respectfully requested.

The aforementioned references, either solely or in combination, also fail to render obvious the claims of the present application. None of the references disclose a method which comprises both the method steps of the present invention, namely using a CD40/CD154 inhibitor and using an additional step of CD154 detection/isolation. As expressly taught by the present specification, the inhibition of CD40 and CD154 interaction allows for larger/longer cell-surface expression of CD154 molecules. As such, a parallel or subsequent CD154-specific detection or isolation of T cells is more efficient. See, the disclosure provided in Example 3 of the present specification and the experimental evidence provided in FIG. 3. As such the subject matter of the present claims is wholly unobvious over the cited Assenmacher, Berner and/or Batataglia references.

The Commissioner is hereby authorized to charge any fees associated with this response to Deposit Account No. 13-3402.

Respectfully submitted,

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